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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,392	11/28/2000	Karen Moore	MPI97-O18CP1DV1M	9536

7590 05/30/2003

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EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 05/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,392	MOORE ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Formal Matters

Claims 16-31 and 47-88 were cancelled in Paper No. 13, 3/11/2003. Claims 32-46 are pending and under consideration.

It is noted that in the response filed 3/11/2003, Applicant included a copy of the pending claims, which were misnumbered as 1-15. The pending claims are 32-46.

Response to Amendment and Arguments

The objection to the title has been withdrawn based on Applicant's amendment.

Applicant's arguments filed in Paper No. 13, 3/11/2003 have been fully considered but they are not persuasive for the reasons set forth below.

Claim Rejections - 35 USC §§ 101, 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-46 stand rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility, for reasons of record set forth in Paper No. 13, 3/11/2003. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the

biological role of this protein or its significance; therefore the claimed method of identifying a compound is not supported by either a credible, specific and substantial asserted utility or a well-established utility. Novel biological molecules lack well-established utility and must undergo extensive experimentation. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

Claims 32-46 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant argues that the Examiner has not met the burden of establishing a prima facie case of lack of utility because the asserted utility of usefulness in diagnostics and therapeutics is based on both homology to GPCRs and tissue expression, and that the function of the I5E polypeptide has been set forth in the art by the publication of Masuda et al. Applicants assert that a prima facie showing must contain the following elements: (i) An explanation that clearly sets forth the reasoning used in concluding that the asserted specific and substantial utility is not credible; (ii) Support for factual findings relied upon in reaching this conclusion; and (iii) An evaluation of all relevant evidence of record, including utilities taught in the closest prior art. In the instant case, the rejection set forth that it was clear from the instant specification that the I5E polypeptide has been assigned a function because of its similarity to known proteins (Specification at 18, line 11).

In the instant case, the I5E protein was found to be a G-protein coupled receptor, however, it is an orphan receptor. Since the ligand to this receptor is unknown, the function of

the protein is also unknown. Neither the specification nor the art of record disclose any diseases or conditions associated with the function or expression of the I5E protein, therefore, there is no "real world" context of use. Further research to identify or reasonably confirm a "real world" context of use is required. In the instant case, the fact that the claimed invention is a method of identifying a compound which modulates a GPCR is not sufficient to establish a specific and substantial utility because there is no specific use of that modulation provided. Applicant argues that the method is useful in diagnosing and treating diseases, but there is no nexus provided by the instant specification to support this use. Although GPCRs have been found to be involved in many different processes and have been the target of much research and drug discovery, unless the specific ligand for each receptor is known, unless the biological activity of the receptor is disclosed or unless the processes and diseases that each receptor is involved in are identified, the method of identifying a compound which modulates a receptor has no "real world" use, and therefore, lacks specific and substantial utility.

Applicant has provided two references that demonstrate that the I5E polypeptide functions as a G protein coupled receptor, and that the ligand for the receptor has been identified. The Masuda et al. reference teaches that I5E is a receptor that binds endocrine gland derived vascular endothelial growth factor (eg-vegf) (see, e.g., page 400, Figure 4). According to MPEP 2107, in order for Applicant to rebut the rejection for lack of utility imposed because the invention lacks an asserted specific and substantial utility for the claimed invention and it does not have a readily apparent well-established utility, Applicant must provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established at the time of filing. The examiner should also ensure that there is an

adequate nexus between the evidence and the properties of the now claimed subject matter as disclosed in the application as filed. That is, the applicant has the burden to establish a probative relation between the submitted evidence and the originally disclosed properties of the claimed invention.

In the instant case, the filing date of the Application is 11/28/2000, with an effective filing date of 4/17/1997. The reference of Masuda et al. that establishes the ligand for the I5E polypeptide has date of publication of April 2002 while WO 200262996A has a publication date of August 15, 2002. Thus, these references which establish the ligand for the I5E receptor are post-filing, and as such, do not provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established at the time of filing. At the time of filing the function of the I5E polypeptide was not known, nor were any specific disease associations known, and these references do not show that the I5E polypeptide had a well-established utility at the time of filing. Additionally, the Masuda et al. reference establishes that the I5E polypeptide binds EG-VEGF and may provide a molecular basis for the regulation of angiogenisis in endocrine glands. However, the specification does not assert that the I5E polypeptide would play a role in angiogenesis or that it would bind EG-VEGF. The specification only asserts that the I5E polypeptide may play a role in metabolic disorders such as obesity, cachexia and anorexia. There is not a correlation between a polypeptide having a role in metabolic disorders such as obesity, cachexia and anorexia and the binding of EG-VEGF and having a role in angiogenesis. Thus, there is not an adequate nexus between the evidence and the properties of the now claimed subject matter as disclosed in the application as filed. The role of the polypeptide as set forth in WO 200262996A could not be evaluated since the abstract only

mentions that the a compound identified in a screen for compounds which alter the binding properties of the polypeptide may be usable in treating or preventing diseases in digestive organs. It is not clear that this establishes a nexus between the assertion in the specification that the I5E polypeptide may play a role in metabolic disorders such as obesity, cachexia and anorexia. Furthermore, the specification did not disclose a specific role that I5E may play in a specific disease, but rather, broadly contemplated a possible role in a disparate listing of many diseases, thus not providing sufficient evidence that a specific and substantial utility based on an association and role in any disease process was known at the time of filing.

Claims 32-46 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if, *arguendo*, the method of identifying a compound to I5E is found to have a patentable utility, claims 38-46 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention, for reasons of record set forth in Paper No. 13, 3/11/2003.

Applicant argues that the claims do not require treatment of a disease, merely identification of compounds that modulate I5E. This is not found persuasive because claims 38-46 specifically recite that the identified compounds must be capable of treating disease, which

treatment is not enabled. The claims as written are directed to identifying compounds which are capable of treating an immune, central nervous system or metabolic disorder, schizophrenia, cognitive disorders multiple sclerosis or depression. In order for the skilled artisan to practice such a method it would be necessary for the artisan to determine the role of I5E in all of these disorders, then design assays for compound identification wherein the compound could modulate the I5E polypeptide such that each and every one of these maladies would be treated. Thus, it would require undue experimentation for one of ordinary skill in the art to practice the claimed invention.

The claims are directed to a method for identifying a compound capable of treating an immune, central nervous system or metabolic disorder, schizophrenia, cognitive disorders, multiple sclerosis or depression by measuring the effect on I5E expression. The specification has not provided the nexus between the etiology of immune, central nervous system or metabolic disorder, schizophrenia, cognitive disorders, multiple sclerosis or depression and I5E expression, and working examples are not provided. The art teaches that recognized methods of treatment of an immune, central nervous system or metabolic disorder, schizophrenia, cognitive disorders, multiple sclerosis or depression in the Merck Manual (pages 1022-1034, 1564-1571, 1474-1476, 1531-1538). The Merck Manual does not disclose the nexus between I5E and an immune, central nervous system or metabolic disorder, schizophrenia, cognitive disorders, multiple sclerosis or depression by measuring the effect on I5E expression.

Since the specification and claims do not disclose the nexus between I5E polypeptide and an immune, central nervous system or metabolic disorder, schizophrenia, cognitive disorders multiple sclerosis or depression, it would require undue experimentation to practice the claimed

method because the skilled artisan would need to determine the role of the I5E polypeptide in each of these disorders, then develop assay systems to identify compounds which would modulate the I5E activity in each of these disorders. Given the breadth of claims 32-46 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to practice the claimed invention.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
May 20, 2003

GARY KUNZ
SUPERVISORY PATENT EXAMINER
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